REMARKS

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Claim Amendments

Claim 4 has been amended to recite a method of protecting the outer retinal layers from damage and/or degeneration. Support for this amendment is found in the Examples of Applicants' specification.

Claim 4 is further amended to recite "full-length recombinant". Support can be found on page 6, line 20 and page 7, lines 25-28 of the specification as filed. Applicants note that recitation of HGF with deletions inherently supports full-length HGF as a base sequence from which deletions and mutations can be made.

No new matter has been added.

Claims 5, 6, 8, 9, 11 and 12 have been cancelled, without prejudice or disclaimer.

Rejections Under 35 U.S.C. § 112, First Paragraph

Written Description

Claims 4-12 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner notes that claims 4-6 recite "decreasing", but no basis for this term has been pointed to and none is apparent.

Applicants respectfully traverse this rejection.

The Examiner states that "while the specification discloses that HGF protects certain structures when administered before damage occurs, the specification does not disclose that HGF can reverse damage that has already occurred."

As stated above, amended claim 4 recites a method for protecting the outer retinal layers from damage and/or degeneration. As acknowledged by the Examiner, the specification supports such a method.

Specifically, Example 1 of the specification demonstrates that administration of HGF prior to light irradiation (in order to prepare light-damaged rats) (1) resulted in more favorable maximum amplitudes and thresholds of the ERG b-wave, compared to the control (see Figures 1 and 2), (2) resulted in a significantly larger nucleic number of rod and cone compared to the

control, and (3) maintained thicknesses of the retinal outer nuclear layer and the photoreceptor layer, compared to the control (see Figure 5).

Furthermore, Example 2 of the specification demonstrates that administration of HGF to Royal College of Surgeon (RCS) rats (1) resulted in significantly more favorable maximum amplitudes and thresholds of the ERG b-wave, compared to the control (see Figures 3 and 4), (2) resulted in significantly larger nucleic numbers, compared to the control, and (3) maintained thicknesses of the retinal outer nuclear layer and the photoreceptor layer (see Figure 6).

As stated on page 12, lines 20-23 of the specification, the Examples demonstrate that HGF protects photoreceptors (rods and cones) in the retinal outer nuclear layer, which are the most important for visual recognition, from degeneration in the retinal light-damaged model and hereditary retina degeneration model.

Additionally, Applicants note that the term "protects" indicates that the HGF is administered *prior to* the damage (e.g., the light irradiation in Example 1).

Thus, the specification clearly provides written description for the method of the amended claims. It is respectfully requested that the above-rejection be withdrawn.

Enablement- HGF

Claims 4-12 are also rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement.

Specifically, the Examiner asserts that the specification exemplifies administering HGF to mice intravitreously prior to retinal damage, wherein the outer retinal layer is disclosed as being protected. However, the Examiner asserts that the particular HGF is not disclosed, and thus, it is now known what species of HGF or whether a full length HGF was used.

Without acquiescence to the correctness of the Examiner's position, claim 4 has been amended to require full-length recombinant HGF. Thus, a person of skill in the art would not have to engage in undue experimentation to practice the claimed invention. It is therefore respectfully requested that the above-rejection be withdrawn.

Enablement- Mode of Administration

Additionally, the Examiner states that the specification only exemplifies intravitreal injection, and does not demonstrate that methods of administration other than intravitreal injection would have been suitably or routinely used for administration of HGF to treat retinopathy.

Applicants respectfully traverse the Examiner's position, because any route of administration that achieves a certain serum level of HGF in blood circulation, i.e., intravenous administration (i.v.), intramuscular administration (i.m.), subcutaneous administration (s.c.), and the like, would be expected to successfully distribute an effective amount of HGF in the retina, thereby yielding the desired pharmacological effect set forth in Applicants' claims.

Enclosed herewith are printouts from two internet sites, which are intended to assist in better understanding the structure of the eye and the choroid. The choroid is a membrane that lies inside the sclera. In the choroid, blood vessels exist to supply oxygen and nutrients to the eyeball and the retina, and when HGF is administered parenterally (e.g., i.v., i.m., s.c.), HGF will reach the retina through the choroid to exhibit the efficacy according to Applicants' claimed method.

The Examiner states that the generic disclosure on pages 7-8 of the specification does not address how different modes of administration will deliver HGF to the appropriate location, namely outer retinal layers, since no blood vessel passes through this region. However, as discussed above, and demonstrated by the enclosed website printouts, one of ordinary skill in this art would understand the structure of the eye and the chloroid, and would understand, based on the disclosure of Applicants' specification and the teachings in the art, that any method of administration which achieves a certain serum level of HGF in the blood would be successful in distributing an effective of amount of HGF to the retina.

Accordingly, Applicants respectfully assert that one of ordinary skill in the art could practice the full scope of the claimed invention, including modes of administration other than intravitreal, without undue experimentation, based upon the teachings of the specification and the knowledge in the art.

Accordingly, it is respectfully requested that the above-rejections be withdrawn.

Consideration After Final Rejection

Although this Amendment is presented after final rejection, the Examiner is respectfully requested to enter the amendments and consider the remarks, as they place the application in condition for allowance.

Rejection Under 35 U.S.C. § 102(b)

The rejection of claims 5, 6, 8, 9, 11 and 12 under 35 U.S.C. § 102(b) as being anticipated by Shibuki et al. has been rendered moot by the cancellation of these claims.

Conclusion

Therefore, in view of the foregoing amendments and remarks, it is submitted that each of the grounds of rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

If, after reviewing this Amendment, the Examiner feels there are any issues remaining which must be resolved before the application can be passed to issue, the Examiner is respectfully requested to contact the undersigned by telephone in order to resolve such issues.

Respectfully submitted,

Shigeki MACHIDA et al.

By /William R. Schmidt, II/

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